

**REMARKS:**

Claims 12-17 are in the case and presented for consideration.

Claim 12 has been amended.

**CLAIM OBJECTIONS**

Claim 12 has been amended in accordance with Examiner's comments and is therefore now believed to be in proper form.

**REJECTION UNDER 35 U.S.C. §112**

Claim 12 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The phrase "being homogeneously distributed" in claim 12 has been replaced with the phrase "being distributed." This new phrase finds support on page 11, lines 31-34 of the originally filed specification.

Therefore, claim 12 is now believed to be in accord with the requirements of 35 U.S.C. §112, first paragraph.

**FIRST REJECTION OF CLAIMS UNDER 35 U.S.C. §103(a)**

Claim 12 was rejected under 35 U.S.C. 103(a) as being unpatentable over the article written by Hampl et al. In the International Journal of Pharmaceutics 144 (1996) 107-114 ("Hampl") in view of U.S. Patent Application 2004/0057970 filed by Domb ("Domb").

Applicants respectfully traverse the Office's rejection that the claims of the present

application are obvious in view of the cited prior art.

Both Hampl and Domb fail to disclose or suggest critical elements claimed in currently amended independent claim 12, from which all other claims depend. Additionally, neither Hampl nor Domb provides a teaching or suggestion which would be sufficient to lead one of ordinary skill in the art to come up with and combine the otherwise missing elements and hence arrive at the invention claimed in currently amended independent claim 12.

Hampl fails to disclose a "biodegradable oligoester" as claimed in currently amended independent claim 12. The oligoesters of the present invention are structurally different from Hampl's co- and terpolymers. This difference is brought about by virtue of the fact that different polycondensation conditions (temperature, pressure, reaction time) are used when preparing the oligoesters of the present invention. The conditions used when preparing the oligoesters of the present invention, allow them to reach a higher degree of branching than Hampl's co- and terpolymers.

Also, Hampl uses, as carrier of its releasing system, co- and terpolymers which are in a solid state under normal temperature and pressure conditions. This is a result of the character of microspheres themselves, and flows from the fact that the microspheres are stored in solid powder form before their medicinal use. Thus, Hampl's co- and terpolymers can not be administered, under normal temperature and pressure conditions, in a plastic state.

By contrast, the oligoesters of the present invention can be administered in a plastic state suitable for forming stable liquid implants under normal temperature and pressure

conditions.

Additionally, Hampl fails to disclose a “viscous” antitumor composition as claimed in currently amended independent claim 12.

Moreover, Hampl, resorts to a releasing system based on microspheres which is notoriously different from that based on the in-situ implant in form of a viscous liquid as used in the present invention.

The respective releasing systems differ from each other not only in the way they are produced and administered, but also in their stability and liberation kinetics. The microspheres of Hampl are produced as two separate components, i.e., powder and dispersion medium. These components are then combined immediately before administration.

By contrast, the in-situ implants of the present invention are prepared in form of viscous liquid ready for instant application. One of the advantages of the implants over the microspheres is that they can be prematurely cleared away in the event of some toxicological, immune or other problem occurring.

Taking into account the above, it is evident that a person skilled in the art working to find a way to administer an antitumor agent in the form of a plastic composition and to create the in-situ implant in form of viscous liquid could not have been able to do so by consulting Hampl. This is the case because Hampl fails to disclose both a polymer carrier which is plastic under normal temperature and pressure conditions and a composition which is capable of being administered as viscous liquid under the same conditions.

Domb also fails to disclose these above mentioned critical elements of currently amended independent claim 12.

It is known that some not negligible local reduction of the pH occurs within tumors of soft tissues. It is also known that these changes increase with the progressive growth of the tumor.

The oligoesters of the present invention, have a relatively low sensitivity to changes in pH of the physiological medium into which the antitumor agent is to be released.

By contrast, the polyanhydrides disclosed in Domb are known to be very sensitive to changes in pH. Once the pH value decreases, the solubility of the degradation products also decrease. This retards the degradation process and has an undesirable impact on the release of antitumor agent. Thus, the polyanhydrides disclosed in Domb are limited to use in brain tissue which is known as an application site having a relatively constant pH value.

Accordingly, if the person skilled in the art had tried, at the time of the: invention, to find a way how to administer an antitumor agent in form of plastic composition to create the in-situ implant in form of viscous liquid within tumors, such a person, would have ignored the content in Domb. In fact, for the above reasons, a person of ordinary skill in the art, when trying to solve the problems addressed by the present invention would be motivated to avoid the teachings in Domb.

In addition, there are further differences between Domb's polyanhydrides and the oligoesters of the present invention which support a finding of non-obviousness with respect to the present invention.

First, ester links are considerably more resistant to hydrolysis than anhydrides. Secondly, because of the relatively low reactivity of the ester links, hydrolysis of polyesters proceeds via a homogeneous erosion throughout the whole volume of the implant.

By contrast, the hydrolysis of polyanhydrides proceeds on the surface of the implant since this reaction is speedier than the diffusion of water into the Implant. This is the called the heterogeneous erosion mechanism. (Lee P I, J. Membr. Sci. 7, 1980, 255-275);

Moreover, with polyanhydrides, the progressive degradation must precede the erosion thereof and as a result, the erosion is strongly dependent on implant geometry (size and form). However, this is not the case when using the oligoesters of the present invention.

Therefore, because both Hampl and Domb either fail to disclose critical claimed elements or teach away from using the critical elements claimed in currently amended independent claims 12, from which all other claims depend, and because neither reference provides a teaching which would lead one of ordinary skill in the art to arrive at the presently claimed invention, the combination of Hampl and Domb does not render any of the present claims obvious.

#### SECOND REJECTION OF CLAIMS UNDER 35 U.S.C. §103(a)

Claims 13-17 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hampl in view of Domb and further in view of U.S. Patent 5,783,205 to Berggren et al. ("Berggren").

The rejection is duly noted but Applicants respectfully traverse this rejection.

As mentioned above, both Hampl and Domb fail to disclose or suggest critical elements claimed in currently amended independent claim 12, from which all other claims

depend. The aforementioned missing element(s) is/are also absent from Berggren. Furthermore, as is the case with Hampl and Domb, Berggren fails to provide a teaching or suggestion which would be sufficient to motivate one of ordinary skill in the art to come up with the otherwise missing element and hence arrive at the invention claimed in currently amended independent claim 12. Furthermore, it has long been a settled matter of law that dependent claims contain all the elements of the claims from which they depend.

Therefore, because the above cited prior art references either fail to disclose critical claimed elements and/or teach away from the presently claimed combination, and because the aforementioned references also fail to provide a teaching, suggestion or motivation which one of ordinary skill in the art could use to arrive at the presently claimed invention, none of the current claims are obvious in light of the combination of Hampl, Domb and Berggren.

Accordingly, the application and claims are believed to be in condition for allowance, and favorable action is respectfully requested.

No new matter has been added.

If any issues remain, the Examiner is respectfully invited to contact the undersigned at the number below, to advance the application to allowance.

Respectfully submitted,  
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